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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,694	09/26/2005	Daniel F Hanley	58719(71699)	2172
49383 7590 07/12/2010 EDWARDS ANGELL PALMER & DODGE LLP P.O. BOX 55874 BOSTON, MA 02205				
EXAMINER				
WEBB, WALTER E				
ART UNIT		PAPER NUMBER		
1612				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/509,694

Applicant(s)

HANLEY ET AL.

Examiner

WALTER E. WEBB

Art Unit

1612

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 May 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 7-17, 22 and 23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 7-17, 22 and 23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)
Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicants' arguments, filed 5/4/2010, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 102--previous

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1) Claims 1-4, 7, 12 and 23 remain rejected under 35 U.S.C. 102(b) as being anticipated by Usui et al., (Neurosurgery 1994).

Usui et al. teaches a method for treating subarachnoid hemorrhage (claims 2-4), in conjunction with external ventricular drainage (claim 7), by administering tPA to human subjects (claim 23) (see Abstract and section titled "Treatment protocol", third paragraph). Solutions of four different concentrations of tPA, 0.042, 0.125, 0.333, and 1mg/10mL, were made and administered (see Id). The injection of tPA was repeated every 6 hours for 5 days (claim 12) (Id.). All patients underwent CT at admission and before surgery, and repeated within 24 hours of surgery, two to three times during and shortly after thrombolytic therapy (see "Radiographic assessment", first paragraph). Patients were treated within 72 hours after SAH (see "Patients and Methods", first

paragraph). Outcome at 3 months after subarachnoid hemorrhage was assessed with the Glasgow Outcome Scale.

Claim Rejections - 35 USC § 103--previous

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 8-11, 13-15 and 22 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Usui et al., (supra) as applied to claims 1-4, 7, 12 and 23 above.

Usui et al., taught above, differs from the instant claims insofar as it does not teach administration between 12-24 or 24-48 hours after diagnosis of the subarachnoid

hemorrhage, performing CT scans at intervals of about 6-24 hours, administering rt-PA about every 4, 10 or 12 hours, or a specific dose of 0.1 mg.

Established precedent holds, even a slight overlap in range establishes a *prima facie* case of obviousness. In re Peterson, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003). Here, a *prima facie* case of obviousness exists where the claimed ranges for treatment after diagnosis of subarachnoid hemorrhage, 12-24 hours and 24-48 hours, lies inside the prior art range of treatment within 72 hours, which is specific enough to reasonably suggest the instantly claimed range for treatment of subarachnoid hemorrhage. Furthermore, Usui et al. teaches that findings have been reported that removal of clot within 48 hours of SAH prevents vasospasm (see first paragraph after Abstract). Accordingly it would have been obvious to have arrived at a time for treatment within the instantly claimed range simply by following the general teachings of Usui et al.

In regard to claim 10, it would have been obvious to perform CT scans at intervals of 6-24 hours to monitor blood clot size, since Usui et al. teaches performing CT scans at admission, before surgery, and repeated within 24 hours of surgery, two to three times during and shortly after thrombolytic therapy. The artisan would have been motivated to use CT to regularly monitor the effects of treatment, especially since tPA has no ability to differentiate a pathological clot from a hemostatic clot.

In regard to claim 13, it would have been obvious to have administered the tPA about every 8 hours, since the Usui et al. teaches administering the thrombolytic agent at 6-8 hour intervals (see Abstract).

In regard to claims 11, 14, 15 and 22, MPEP 2131.03 states that a *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. Here, the administering rt-PA about every 4, 10 or 12 hours is *prima facie* obvious insofar as it is reasonably close enough to every 6-8 hours such that one skilled in the art would have expected them to have the same properties. A *prima facie* case of obviousness also exists in regard to the administration of a 0.1mg dose (claim 22), since Usui teaches administering a dose of rt-PA at 0.133mg, which is reasonable close enough that one skilled in the art would have expected them to have the same properties.

2) Claims 16 and 17 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Usui et al., (supra) as applied to claims 1-4, 7, 12 and 23 above, and in further view of Mayfrank et al., (Acta Neurochir (Wien) 1993).

Usui et al. differs from the instant claims 16 and 17 insofar as it does not teach stopping treatment when the blood clot is 80% of its original size, or when the blood clot is 80% of its original size about 3 days after the first administration of the thrombolytic agent.

Mayfrank et al. teaches a method of treating blood clots in the brain by administering rtPA. (See Abstract.) The reference teaches that rtPA has been known to lyse subarachnoid blood clots. (See pg. 32, right column, 4th paragraph.) Mayfrank teaches stopping treatment until CT scans demonstrate a substantial reduction of

intraventricular blood (see pg. 32, left col., 1st paragraph). Mayfrank taught that ventricular size decrease was normal in all patients after 48 hours of treatment, and that the resolution of accompanying intraventricular haematomas (clots) seemed not to be accelerated by intraventricular rtPA injection. (See pg. 34, left col., 1st paragraph.)

It would have also been obvious to stop treatment when the blood clot is 80% of its original size in the method of Usui et al., since treatment includes drainage and an 80% blood clot reduction may be small enough to be eliminated by the drainage within the first three days of treatment. If all or a substantial portion of the blood has been removed from the ventricle, there would be no need for further treatment, as taught by Mayfrank et al.

Response to Amendment

Applicant has amended claim 1 to recite the phrase, "wherein the subject can be assessed using the Glasgow Coma Scale." However, this amendment does not overcome the art of record in regard to Usui et al., since the patients are adults, there mean age being 58.6 +/- 11.8, and therefore can be assessed using the Glasgow Coma Scale.

Response to Arguments

Applicant argues that Usui et al. does not anticipate claims 2 and 3, stating that the subarachnoid space is outside the brain, adjacent to the pia matter, while the intraventricular space and the intracerebral space are both within the brain. However, the instant claims 2 and 3 are not drawn to treating a blood clot in the brain. The claims

require treating an extravascular hematoma, which means outside the vasculature. Claims 2 and 3 further limit the type of clot by indicating that it is “associated with intraventricular hemorrhage” (claim 2) and “associated with intracerebral hemorrhage” (claim 3). Usui et al. clearly teaches treating subarachnoid and intraventricular clots with tPA, which are inevitably associated with intraventricular hemorrhage and intraventricular hemorrhage. Further, the subarachnoid hemorrhages of Usui et al., i.e. bleeding in the subarachnoid spaces, resulted from ruptured cerebral aneurysms, which are inherently intracerebral hemorrhages. The blood clots of Usui et al. were also associated with intraventricular hemorrhage insofar as the method of treating the hematomas involved using, as necessary, a ventricular catheter to withdraw the hematomas. The reference also taught treating a patient who subsequently developed intraventricular hemorrhage during therapy.

In regard to excluding patients with intracerebral and or intraventricular hemorrhage, Usui et al. stated that these patients also had no blood clot at the basal subarachnoid spaces, i.e. no subarachnoid hemorrhage. The purpose of the study was to prevent vasospasms associated with subarachnoid hemorrhage (see Title). It would only make sense to exclude patients that did not exhibit a subarachnoid hemorrhage since they would not be expected to develop vasospasms.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 8:00am-4:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Walter E. Webb
/Walter E Webb/
Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612